

# SEQUENCE LISTING

<110> Commonwealth Scientific and Industrial Research  
 Organisation  
 Walter and Eliza Hall Institute of Medical Research  
 Ludwig Institute for Cancer Research

<120> Crystal structure of ErbB2 and uses thereof

<130> 501742/JEP

<150> Australian Patent Provisional Application No 2002951853  
 <151> 2002-10-04

<160> 4

<170> PatentIn version 3.1

<210> 1  
 <211> 509  
 <212> PRT  
 <213> Homo sapiens

<400> 1

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Thr | Gln | Val | Cys | Thr | Gly | Thr | Asp | Met | Lys | Leu | Arg | Leu | Pro | Ala |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Ser | Pro | Glu | Thr | His | Leu | Asp | Met | Leu | Arg | His | Leu | Tyr | Gln | Gly | Cys |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Gln | Val | Val | Gln | Gly | Asn | Leu | Glu | Leu | Thr | Tyr | Leu | Pro | Thr | Asn | Ala |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Ser | Leu | Ser | Phe | Leu | Gln | Asp | Ile | Gln | Glu | Val | Gln | Gly | Tyr | Val | Leu |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Ile | Ala | His | Asn | Gln | Val | Arg | Gln | Val | Pro | Leu | Gln | Arg | Leu | Arg | Ile |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Val | Arg | Gly | Thr | Gln | Leu | Phe | Glu | Asp | Asn | Tyr | Ala | Leu | Ala | Val | Leu |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Asp | Asn | Gly | Asp | Pro | Leu | Asn | Asn | Thr | Thr | Pro | Val | Thr | Gly | Ala | Ser |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Pro | Gly | Gly | Leu | Arg | Glu | Leu | Gln | Leu | Arg | Ser | Leu | Thr | Glu | Ile | Leu |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     |     | 125 |     |     |

Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln Leu Cys Tyr Gln Asp  
130 135 140

Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu  
145 150 155 160

Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro  
165 170 175

Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln  
180 185 190

Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala Arg Cys Lys Gly  
195 200 205

Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr  
210 215 220

Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn His Ser  
225 230 235 240

Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp  
245 250 255

Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala  
260 265 270

Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu Ser Thr Asp Val Gly  
275 280 285

Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln Glu Val Thr Ala Glu  
290 295 300

Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val  
305 310 315 320

Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr  
325 330 335

Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser  
340 345 350

Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr

|   |     |         |
|---|-----|---------|
| 355   | 360 | 365     |
| Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu |     |         |
| 370   | 375 | 380     |
| Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro Asp |     |         |
| 385   | 390 | 395 400 |
| Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His |     |         |
| 405   | 410 | 415     |
| Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu |     |         |
| 420   | 425 | 430     |
| Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His |     |         |
| 435   | 440 | 445     |
| His Asn Thr His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu |     |         |
| 450   | 455 | 460     |
| Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro Glu |     |         |
| 465   | 470 | 475 480 |
| Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His Gln Leu Cys Ala Arg |     |         |
| 485   | 490 | 495     |
| Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn             |     |         |
| 500   | 505 |         |
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| <211> 501   |     |         |
| <212> PRT   |     |         |
| <213> Homo sapiens  |     |         |
| <400> 2   |     |         |
| Leu Glu Glu Lys Lys Val Cys Gln Gly Thr Ser Asn Lys Leu Thr Gln |     |         |
| 1   | 5   | 10 15   |
| Leu Gly Thr Phe Glu Asp His Phe Leu Ser Leu Gln Arg Met Phe Asn |     |         |
| 20  | 25  | 30      |
| Asn Cys Glu Val Val Leu Gly Asn Leu Glu Ile Thr Tyr Val Gln Arg |     |         |
| 35  | 40  | 45      |

Asn Tyr Asp Leu Ser Phe Leu Lys Thr Ile Gln Glu Val Ala Gly Tyr  
50 55 60

Val Leu Ile Ala Leu Asn Thr Val Glu Arg Ile Pro Leu Glu Asn Leu  
65 70 75 80

Gln Ile Ile Arg Gly Asn Met Tyr Tyr Glu Asn Ser Tyr Ala Leu Ala  
85 90 95

Val Leu Ser Asn Tyr Asp Ala Asn Lys Thr Gly Leu Lys Glu Leu Pro  
100 105 110

Met Arg Asn Leu Gln Glu Ile Leu His Gly Ala Val Arg Phe Ser Asn  
115 120 125

Asn Pro Ala Leu Cys Asn Val Glu Ser Ile Gln Trp Arg Asp Ile Val  
130 135 140

Ser Ser Asp Phe Leu Ser Asn Met Ser Met Asp Phe Gln Asn His Leu  
145 150 155 160

Gly Ser Cys Gln Lys Cys Asp Pro Ser Cys Pro Asn Gly Ser Cys Trp  
165 170 175

Gly Ala Gly Glu Glu Asn Cys Gln Lys Leu Thr Lys Ile Ile Cys Ala  
180 185 190

Gln Gln Cys Ser Gly Arg Cys Arg Gly Lys Ser Pro Ser Asp Cys Cys  
195 200 205

His Asn Gln Cys Ala Ala Gly Cys Thr Gly Pro Arg Glu Ser Asp Cys  
210 215 220

Leu Val Cys Arg Lys Phe Arg Asp Glu Ala Thr Cys Lys Asp Thr Cys  
225 230 235 240

Pro Pro Leu Met Leu Tyr Asn Pro Thr Thr Tyr Gln Met Asp Val Asn  
245 250 255

Pro Glu Gly Lys Tyr Ser Phe Gly Ala Thr Cys Val Lys Lys Cys Pro  
260 265 270

Arg Asn Tyr Val Val Thr Asp His Gly Ser Cys Val Arg Ala Cys Gly  
275 280 285

Ala Asp Ser Tyr Glu Met Glu Glu Asp Gly Val Arg Lys Cys Lys Lys  
290 295 300

Cys Glu Gly Pro Cys Arg Lys Val Cys Asn Gly Ile Gly Ile Gly Glu  
305 310 315 320

Phe Lys Asp Ser Leu Ser Ile Asn Ala Thr Asn Ile Lys His Phe Lys  
325 330 335

Asn Cys Thr Ser Ile Ser Gly Asp Leu His Ile Leu Pro Val Ala Phe  
340 345 350

Arg Gly Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu Leu  
355 360 365

Asp Ile Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile Gln  
370 375 380

Ala Trp Pro Glu Asn Arg Thr Asp Leu His Ala Phe Glu Asn Leu Glu  
385 390 395 400

Ile Ile Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala Val  
405 410 415

Val Ser Leu Asn Ile Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu Ile  
420 425 430

Ser Asp Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala  
435 440 445

Asn Thr Ile Asn Trp Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys Thr  
450 455 460

Lys Ile Ile Ser Asn Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly Gln  
465 470 475 480

Val Cys His Ala Leu Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu Pro  
485 490 495

Arg Asp Cys Val Ser  
500

<210> 3  
<211> 500  
<212> PRT  
<213> Homo sapiens

<400> 3

Ser Glu Val Gly Asn Ser Gln Ala Val Cys Pro Gly Thr Leu Asn Gly  
1 5 10 15

Leu Ser Val Thr Gly Asp Ala Glu Asn Gln Tyr Gln Thr Leu Tyr Lys  
20 25 30

Leu Tyr Glu Arg Cys Glu Val Val Met Gly Asn Leu Glu Ile Val Leu  
35 40 45

Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile Arg Glu Val  
50 55 60

Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Thr Leu Pro Leu  
65 70 75 80

Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp Gly Lys Phe  
85 90 95

Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser His Ala Leu  
100 105 110

Arg Gln Leu Arg Leu Thr Gln Leu Thr Glu Ile Leu Ser Gly Gly Val  
115 120 125

Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr Ile Asp Trp  
130 135 140

Arg Asp Ile Val Arg Asp Arg Asp Ala Glu Ile Val Val Lys Asp Asn  
145 150 155 160

Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly Arg Cys Trp  
165 170 175

Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr Ile Cys Ala  
180 185 190

Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn Gln Cys Cys  
195 200 205

His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp Thr Asp Cys  
210 215 220

Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val Pro Arg Cys  
225 230 235 240

Pro Gln Pro Leu Val Tyr Asn Lys Leu Thr Phe Gln Leu Glu Pro Asn  
245 250 255

Pro His Thr Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala Ser Cys Pro  
260 265 270

His Asn Phe Val Val Asp Gln Thr Ser Cys Val Arg Ala Cys Pro Pro  
275 280 285

Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys Glu Pro Cys  
290 295 300

Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser Gly Ser Arg  
305 310 315 320

Phe Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val Asn Cys Thr  
325 330 335

Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu Asn Gly Asp  
340 345 350

Pro Trp His Lys Ile Pro Ala Leu Asp Pro Glu Lys Leu Asn Val Phe  
355 360 365

Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln Ser Trp Pro  
370 375 380

Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr Thr Ile Gly  
385 390 395 400

Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile Met Lys Asn  
405 410 415

Leu Asn Val Thr Ser Leu Gly Phe Arg Ser Leu Lys Glu Ile Ser Ala  
420 425 430

Gly Arg Ile Tyr Ile Ser Ala Asn Arg Gln Leu Cys Tyr His His Ser  
435 440 445

Leu Asn Trp Thr Lys Val Leu Arg Gly Pro Thr Glu Glu Arg Leu Asp  
450 455 460

Ile Lys His Asn Arg Pro Arg Arg Asp Cys Val Ala Glu Gly Lys Val  
465 470 475 480

Cys Asp Pro Leu Cys Ser Ser Gly Gly Cys Trp Gly Pro Gly Pro Gly  
485 490 495

Gln Cys Leu Ser  
500

<210> 4  
<211> 502  
<212> PRT  
<213> Homo sapiens

<400> 4

Gln Pro Ser Asp Ser Gln Ser Val Cys Ala Gly Thr Glu Asn Lys Leu  
1 5 10 15

Ser Ser Leu Ser Asp Leu Glu Gln Gln Tyr Arg Ala Leu Arg Lys Tyr  
20 25 30

Tyr Glu Asn Cys Glu Val Val Met Gly Asn Leu Glu Ile Thr Ser Ile  
35 40 45

Glu His Asn Arg Asp Leu Ser Phe Leu Arg Ser Val Arg Glu Val Thr  
50 55 60

Gly Tyr Val Leu Val Ala Leu Asn Gln Phe Arg Tyr Leu Pro Leu Glu  
65 70 75 80

Asn Leu Arg Ile Ile Arg Gly Thr Lys Leu Tyr Glu Asp Arg Tyr Ala  
85 90 95

Leu Ala Ile Phe Leu Asn Tyr Arg Lys Asp Gly Asn Phe Gly Leu Gln



|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|
|     | 100 |     | 105 |     | 110 |     |     |     |     |     |     |     |     |     |     |  |  |  |  |
| Glu | Leu | Gly | Leu | Lys | Asn | Leu | Thr | Glu | Ile | Leu | Asn | Gly | Gly | Val | Tyr |  |  |  |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |  |  |  |
| Val | Asp | Gln | Asn | Lys | Phe | Leu | Cys | Tyr | Ala | Asp | Thr | Ile | His | Trp | Gln |  |  |  |  |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |  |  |  |
| Asp | Ile | Val | Arg | Asn | Pro | Trp | Pro | Ser | Asn | Leu | Thr | Leu | Val | Ser | Thr |  |  |  |  |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |  |  |  |
| Asn | Gly | Ser | Ser | Gly | Cys | Gly | Arg | Cys | His | Lys | Ser | Cys | Thr | Gly | Arg |  |  |  |  |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |  |  |  |  |
| Cys | Trp | Gly | Pro | Thr | Glu | Asn | His | Cys | Gln | Thr | Leu | Thr | Arg | Thr | Val |  |  |  |  |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |  |  |  |
| Cys | Ala | Glu | Gln | Cys | Asp | Gly | Arg | Cys | Tyr | Gly | Pro | Tyr | Val | Ser | Asp |  |  |  |  |
|     | 195 |     |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |  |  |  |
| Cys | Cys | His | Arg | Glu | Cys | Ala | Gly | Gly | Cys | Ser | Gly | Pro | Lys | Asp | Thr |  |  |  |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |  |  |  |
| Asp | Cys | Phe | Ala | Cys | Met | Asn | Phe | Asn | Asp | Ser | Gly | Ala | Cys | Val | Thr |  |  |  |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |  |  |  |
| Gln | Cys | Pro | Gln | Thr | Phe | Val | Tyr | Asn | Pro | Thr | Thr | Phe | Gln | Leu | Glu |  |  |  |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |  |  |  |
| His | Asn | Phe | Asn | Ala | Lys | Tyr | Thr | Tyr | Gly | Ala | Phe | Cys | Val | Lys | Lys |  |  |  |  |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |  |  |  |  |
| Cys | Pro | His | Asn | Phe | Val | Val | Asp | Ser | Ser | Ser | Cys | Val | Arg | Ala | Cys |  |  |  |  |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |  |  |  |
| Pro | Ser | Ser | Lys | Met | Glu | Val | Glu | Glu | Asn | Gly | Ile | Lys | Met | Cys | Lys |  |  |  |  |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |  |  |  |
| Pro | Cys | Thr | Asp | Ile | Cys | Pro | Lys | Ala | Cys | Asp | Gly | Ile | Gly | Thr | Gly |  |  |  |  |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |  |  |  |  |
| Ser | Leu | Met | Ser | Ala | Gln | Thr | Val | Asp | Ser | Ser | Asn | Ile | Asp | Lys | Phe |  |  |  |  |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |  |  |  |  |

Ile Asn Cys Thr Lys Ile Asn Gly Asn Leu Ile Phe Leu Val Thr Gly  
340 345 350

Ile His Gly Asp Pro Tyr Asn Ala Ile Glu Ala Ile Asp Pro Glu Lys  
355 360 365

Leu Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Phe Leu Asn Ile  
370 375 380

Gln Ser Trp Pro Pro Asn Met Thr Asp Phe Ser Val Phe Ser Asn Leu  
385 390 395 400

Val Thr Ile Gly Gly Arg Val Leu Tyr Ser Gly Leu Ser Leu Leu Ile  
405 410 415

Leu Lys Gln Gln Gly Ile Thr Ser Leu Gln Phe Gln Ser Leu Lys Glu  
420 425 430

Ile Ser Ala Gly Asn Ile Tyr Ile Thr Asp Asn Ser Asn Leu Cys Tyr  
435 440 445

Tyr His Thr Ile Asn Trp Thr Thr Leu Phe Ser Thr Ile Asn Gln Arg  
450 455 460

Ile Val Ile Arg Asp Asn Arg Lys Ala Glu Asn Cys Thr Ala Glu Gly  
465 470 475 480

Met Val Cys Asn His Leu Cys Ser Ser Asp Gly Cys Trp Gly Pro Gly  
485 490 495

Pro Asp Gln Cys Leu Ser  
500